REMARKS

With the entry of the present Amendment, claims 79-85 and 88-95 are in this application. Claim 90 has been amended to correct an inadvertent typographical error. None of the amendments made herein constitutes the addition of new matter.

The Rejections under 35 U.S.C. 112, second paragraph

Claims 79-81, 85 and 88-95 have been rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite. Applicants respectfully traverse this rejection.

Claims 79-81 and 90 have been rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite in the recitation of "consisting essentially of" with respect to nucleotide or amino acid sequences. The Patent Office has alleged that this term is not defined in the Specification.

Applicants respectfully submit that the use of "consisting essential of" is well understood in patent drafting to mean that there cannot be additional materials that materially affect the basic and novel characteristic of the claimed invention. See the MPEP at 2111.03 and case law including In re Hertz, 190 USPQ 461, CCPA 1976), as well as other more recent decisions. The critical aspect of the claimed invention is the referenced sequence, and additional associated nucleotides (or small variations in the recited sequence) should be permitted, provided they do not change the function of the recited sequence. Therefore, the claims are not properly deemed indefinite.

Claims 85 and 95 have been deemed indefinite in the recitation of "substantially identical." It has been alleged that the Specification does not define this recitation. Claims 88 and 89 were included because they depend from these claims.

Applicants respectfully point the Examiner to the Substitute Specification, page 23, lines 19-22, where "substantially identical is defined to include any sequence which is at

least about 95% identical..." Because the Specification provides a definition, it follows that the Patent Office should view these claims as definite and allow them.

Accordingly, the withdrawal of the rejection is respectfully requested.

The Rejections under 35 U.S.C. 112, first paragraph

Claims 79-81, 85 and 88-95 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly not enabled for coding sequences which consist essentially of or are substantially identical to the specifically exemplified sequences. Applicants respectfully traverse this rejection.

The meanings and interpretations of "substantially identical" and "consisting essentially of" in the context of the present claims has been discussed above. Claims ... include functional limitations (bind ecdysone, etc) and the structure is limited in terms of substantially identical to or consisting essentially of a recited sequence.

Exhibits A and B from the prior amendment are submitted herewith. These exhibits, are again discussed below.

The Examiner indicated in an informal telephone interview that examples of ecdysone receptors of at least 60% sequence identity to SEQ ID NO:10 would overcome the rejection. Applicants provide herewith the results of sequence comparisons in which two ecdysone receptor clones from *Nezara virdula* show 72.9 and 73.4% sequence identity to the exemplified SEQ ID NO:10 ecdysone receptor of *Myzus persicae*. See Exhibit A for a summary of these sequence comparisons. In addition, the ecdysone receptor from *Bemesia tabacai* shows 71.6% amino acid sequence identity to SEQ ID NO:10. See Exhibit B for the results of this sequence comparison. Accordingly, Applicants respectfully request withdrawal of the rejection. As argued previously, Applicants have provided adequate description – with respect to sequence relatedness and with the provision of an

ecdysone binding assay readily carried out by one of ordinary skill in the art. Applicants maintain on the record that there would be no requirement for **undue** experimentation. One of ordinary skill in the art would be unlikely to construct random variants of the recited sequences and then test for binding activity, but rather one of ordinary skill in the art would be most likely to look to expressed sequences in an insect where ecdysone hormones are present. The required functional activity of an ecdysone receptor protein has been clearly set forth: ecdysone binding activity.

The Patent Office has further characterized the state of the art as being that "even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function, and that a single amino acid change in a protein's sequence can drastically affect the structure of a protein and the architecture of an entire cell," citing the example of sickle cell anemia.

Applicants have already amended claims 85 and 95 to recite sequences substantially identical to the specifically exemplified sequence. This is supported by page 23, lines 19-22 of the substitute specification. Although the Examiner makes statements relative to the potential importance of single amino acid changes, Applicants respectfully maintain that the art can readily make substitution mutations and test them, and only those sequences which encode a protein which binds ecdysteroid are within the scope of the claims.

In view of the high level of skill in the relevant art, the well known techniques for identifying sequences with the specified relatedness to the specific sequence, and the readily accessible methods for testing a protein for ligand binding (e.g., ecdysone binding), Applicants respectfully urge that the invention as claimed is adequately enabled by the as-filed Specification, taken with what is well known and readily accessible in the art.

Claims 79-81, 85 and 89-95 have been rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement, with the Patent Office alleging the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed, had possession of the invention. Applicants respectfully traverse this rejection.

As stated above, claims 79-84 and 91-94 recite specifically the exemplified sequences set forth in SEQ ID NOs:9 and 10 and/or SEQ ID NOs:11 and 12. With respect to the remaining claims, there are structural and functional limitations in the claims. Ecdysone binding is determined using techniques well known to the art. Proteins which do not, in the appropriate heterodimer, bind ecdysone are outside the metes and bounds of the claims. The application, at page 38, line 23, through page 39, line 2, provides guidance concerning conservative acid substitutions. This is well understood in the art, and variants produced can be tested using techniques well known to the art. Applicants respectfully maintain that the claims are adequately enabled when the Specification is taken together with the knowledge of the art.

Applicants respectfully maintain that the claims are adequately enabled when the Specification is taken together with the knowledge of the art.

Claims 93-94 have been rejected under 35 U.S.C. 112, first paragraph, as the Specification is alleged to enable a cultured or isolated host cell but not "host cells". Applicants respectfully traverse this rejection.

The Patent Office has provided a number of references which address the potential failure to express a sequence of the present invention in certain possible host cells. However, Applicants respectfully maintain that the preponderance of host cells into which an expression vector carrying a coding sequence of the present operably linked to

transcription regulatory sequences appropriate to a host cell in question, will exhibit expression of the particular coding sequence. Applicants respectfully maintain the preponderant number of successful host cell types actually meet the requirement of the Atlas Powder v. DuPont case cited by the Patent Office.

The level of skill in the relevant art is very high and there is more than twenty years of experience in gene expression on which to draw. A patent needn't teach and is preferred to omit what is well known and readily accessible to the art, according to case law including Hybritech v. Monoclonal Antibodies, 231 USPQ 81, CAFC, 1986.

No et al. (1996) "Ecdysone-inducible gene expression in mammalian cells and transgenic mice," Proc. Natl. Acad. Sci. USA 93:3346-3351, submitted herewith as Exhibit C, describes transgenic mammalian cell and mice in which insect transcription regulatory sequences are functional when the ecdysteroid receptor is expressed to mediate response to externally administered ecdysteroids. This supports the breadth of the existing claims. The transgenic animal art (and corresponding plant art as well) knows how to introduce heterologous genes for expression in a genetically modified cell or animal or plant of choice, and there is nothing apparent about the particular coding sequences of the present invention that would suggest problems with their expression in cells or organisms other than those in which they occur in nature. Accordingly, Applicants have not amended the claims to recite "isolate" host cell at this time.

Bender et al. (1997) "Drosophila ecdysone receptor mutations reveal functional differences among receptor isoforms," Cell 91:777-788, submitted as Exhibit D, appears to teach the characterization of a variety of mutations in the ecdysone receptor(s) of Drosophila.

In view of the amendments to the claims and the foregoing discussion, Applicants respectfully request the withdrawal of the rejections under 35 U.S.C. 112, first paragraph.

Conclusion

In view of the foregoing, it is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This amendment is accompanied by a Petition for Extension of Time (three months) and authorization to charge the amount of $1020.00 to Deposit No. 07-1969 as required by 37 C.F.R. 1.17(a). It is believed that this amendment does not necessitate the payment of any additional fees under 37 C.F.R. 1.16-1.17, but if the amount authorized is incorrect, please charge the appropriate amount to Deposit No. 07-1969.

Respectfully submitted,

/donnamferber/

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